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1653 470

DATE: 12/17/2001

TIME: 10:43:45

Input Set : A:\MSB-7255.1.txt

PATENT APPLICATION: US/10/006,091

RAW SEQUENCE LISTING

Output Set: N:\CRF3\12172001\J006091.raw

```
3 <110> APPLICANT: Cho, Myung-Sam
                                                                     FNTERE
             Chan, Sham-Yuen
             Kelsey, William
             Yee, Helena
     8 <120> TITLE OF INVENTION: Expression System for Factor VIII
    10 <130> FILE REFERENCE: MSB-7255.1
C--> 12 <140> CURRENT APPLICATION NUMBER: US/10/006,091
C--> 13 <141> CURRENT FILING DATE: 2001-12-06
    15 <160> NUMBER OF SEQ ID NOS: 2
    17 <170> SOFTWARE: PatentIn Ver. 2.0
    19 <210> SEQ ID NO: 1
    20 <211> LENGTH: 1438
    21 <212> TYPE: PRT
    22 <213> ORGANISM: Artificial Sequence
    24 <220> FEATURE:
    25 <223> OTHER INFORMATION: Description of Artificial Sequence: Derived from
             human factor VIII sequence
    28 <400> SEQUENCE: 1
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    35 Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val Tyr Lys Lys
    38 Thr Leu Phe Val Glu Phe Thr Val His Leu Phe Asn Ile Ala Lys Pro
                                 55
    41 Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln Ala Glu Val
                                                 75
    44 Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro Val
                        85
                                            90
    47 Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly Ala
                   100
                                       105
    50 Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys Val
                                    120
    53 Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn
                               135
    56 Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser Tyr Leu Ser
                           150
    59 His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile Gly Ala Leu
    60
    62 Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr Gln Thr Leu
                   180
                                       185
    65 His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser Trp
                                   200
    68 His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala Ser
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215

71 Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg

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Input Set : A:\MSB-7255.1.txt

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70	225					220					225					240
	225	-	_	a 1.	.	230	a 1	a	77.5 -	7	235	0	170 1		III 20 20	
	ser	Leu	Pro	Gly		TTE	GIY	Cys	HIS		ьys	ser	Val	туг		HIS
75	1	~ 1	a 1		245	en la ca	m1	D	01	250	***	a	-1 -	Db -	255	a 1
	Val	He	GTA	Met	GLY	Thr	Thr	Pro		vaı	HIS	ser	тте		Leu	GIU
78			_,	260	_		_	_	265	_	-1		_	270	~ 1	-1
	Gly	His		Phe	Leu	Val	Arg		His	Arg	GIn	Ala		Leu	Glu	TTE
81			275					280			_	_	285	_		-1
	Ser		Ile	Thr	Phe	Leu		Ala	Gln	Thr	Leu		Met	Asp	Leu	GIY
84		290					295					300			_	
		Phe	Leu	Leu	Phe	_	His	Ile	Ser	Ser		Gln	His	Asp	Gly	
	305					310					315					320
89	Glu	Ala	Tyr	Val		Val	Asp	Ser	Cys		Glu	Glu	Pro	Gln		Arg
90					325					330					335	
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93				340					345					350		
95	Ser	Glu	Met	Asp	Val	Val	Arg	Phe	Asp	Asp	Asp	Asn	Ser	Pro	Ser	Phe
96			355					360					365			
98	Ile	Gln	Ile	Arg	Ser	Val	Ala	Lys	Lys	His	Pro	Lys	\mathtt{Thr}	Trp	Val	His
99		370					375					380				
101	Tyr	Ile	ala	a Ala	Glu	ı Glu	ı Glu	Asp	Trp	Asp	Туг	Ala	Pro	Let	ı Va]	Leu
	385					390					395					400
104	Ala	Pro	Asp	Asp	Arg	, Ser	Tyr	Lys	s Sei	Gln	Туі	Leu	Asr	Asr	Gly	7 Pro
105					405	5				410)				415	5
107	Glr	Arg	, Ile	e Gly	Arg	, Lys	Tyr	Lys	Lys	val	. Arg	, Phe	Met	: Ala	туз	Thr
108				420)				425	;				430	}	
110	Asp	Glu	ı Thr	? Phe	Lys	Thr	Arg	Glu	ı Ala	ıle	: Glr	n His	Glu	Ser	: Gly	Ile
111			435	5				440)				445	;		
113	Leu	Gly	Pro	Leu	Leu	Tyr	Gly	Glu	ı Val	. Gly	Asp	Thr	Leu	Lev	11e	e Ile
114		450)				455	,				460	ļ.			
116	Phe	Lys	Asn	Gln	Ala	Ser	Arg	Pro	туг	Asn	Ile	Yyr	Pro	His	Gly	, Ile
117	465	,				470	ļ				475	5				480
119	Thr	Asp	val	. Arg	Pro	Leu	Tyr	Ser	Arg	, Arg	Leu	Pro	Lys	Gly	val	Lys
120					485	;				490	l				495	5
122	His	Leu	Lys	Asp	Phe	Pro	Ile	Leu	ı Pro	Gly	Glu	ılle	Phe	Lys	туг	Lys
123				500					505	j				510)	
125	Trp	Thr	. Val	. Thr	Val	. Glu	Asp	Gly	Pro	Thr	Lys	Ser	Asp	Pro	Arg	Cys
126			515	i				520)				525	i		
128	Leu	Thr	Arg	Tyr	Tyr	Ser	Ser	Phe	val	Asn	Met	: Glu	Arg	Asp	Leu	ı Ala
129		530					535					540	ı			
131	Ser	Gly	Leu	ı Ile	Gly	Pro	Leu	Leu	ı Ile	Cys	Tyr	Lys	Glu	Ser	· Val	Asp
132	545					550					555	,				560
			Gly	Asn	Gln	ılle	Met	Ser	Asp	Lys	Arg	Asn	Val	Ile	Let	l Phe
135		,	_		565				-	570					575	
		Val	Phe	Asp	Glu	Asn	Arq	Ser	Trp	Tyr	Leu	Thr	Glu	Asn	Ile	e Gln
138				580			,		585					590		
		Phe	Leu	Pro	Asn	Pro	Ala	Gly	val	Gln	Leu	Glu	Asp	Pro	Glu	ı Phe
141	_		595					600					605			
143	Gln	Ala	Ser	Asn	Ile	Met	His	Ser	: Ile	Asn	Gly	Tyr	Val	Phe	Asp	Ser
144		610					615				_	620			_	

RAW SEQUENCE LISTING DATE: 12/17/2001 PATENT APPLICATION: US/10/006,091 TIME: 10:43:45

Input Set : A:\MSB-7255.1.txt

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	Leu	Gln	Leu	Ser	Val	_	Leu	His	Glu	Val		Tyr	Trp	Tyr	Ile	
	625					630					635				_	640
149	Ser	Ile	Gly	Ala	Gln	Thr	Asp	Phe	Leu	Ser	Val	Phe	Phe	Ser	Gly	${ t Tyr}$
150					645					650					655	
152	Thr	Phe	Lys	His	Lys	Met	Val	Tyr	Glu	Asp	Thr	Leu	Thr	Leu	Phe	Pro
153			_	660	_			_	665					670		
	Phe	Ser	Glv	Glu	Thr	Va l	Phe	Met	Ser	Met	Glu	Asn	Pro	Glv	Leu	Trp
156	1 110	001	675					680					685	1		1
	Ile	T 011		Crra	ui c	7 an	Cor		Dho	λνα	λαn	Ara		Mot	Thr	Λla
	тте		GLY	Cys	птэ	ASII		ASP	Pne	AIG	HSII		GIY	Mec	1111	Ата
160	_	690	_	1			695					700		m	m	a 1
	Leu	Leu	ьуs	vaı	ser		Cys	ASP	гàг	Asn		GIY	Asp	TYL	TAT	
	705					710		_			715					720
165	Asp	Ser	Tyr	Glu	Asp	Ile	Ser	Ala	Tyr	Leu	Leu	Ser	Lys	Asn	Asn	Ala
166					725					730					735	
168	Ile	Glu	Pro	Arg	Ser	Phe	Ser	Gln	Asn	Pro	Pro	Val	Leu	Lys	Arg	His
169				740					745					750		
171	Gln	Arg	Glu	Ile	Thr	Arq	Thr	Thr	Leu	Gln	Ser	Asp	Gln	Glu	Glu	Ile
172		_	755					760					765			
174	Asp	Tvr	Asp	Asp	Thr	Ile	Ser	Val	Glu	Met	Lvs	Lvs	G1u	Asp	Phe	Asp
175		770					775				4	780				-
	Ile		Agn	Glu	Asn	Glu		Gln	Ser	Pro	Ara		Phe	G1 n	Lvs	Lvs
	785	- <i>1</i> -	nop	014	7100	790	11011	0111	001	110	795	JU1	- 110	02	272	800
	Thr	λκα	uic	mazz.	Dho		7 J a	7 T =	17 = 1	Glu		Lau	Trn	Nen	Titan	
	T 111	ALY	птъ	ıyı	805	116	мта	AIU	val	810	ALY	пец	пр	кэр	815	GIY
181	14.4	a	a	a	-	77.5	77.0.1	T	1		7	77-	C1 n	Com		Com
	Met	ser	ser		PLO	HIS	Val	ren	-	ASII	Arg	Ald	GIII		СТА	ser
184	3	_		820	_	_			825	~ 3	-1	-1	1	830	a 1	a .
	Val	Pro		Phe	Lys	Lys	Val		Phe	GIn	Glu	Phe		Asp	GTA	ser
187			835					840	_				845		_	
189	Phe	Thr	G1n	Pro	Leu	${ t Tyr}$	Arg	Gly	Glu	Leu	Asn	Glu	His	Leu	Gly	Leu
190		850					855					860				
192	Leu	Gly	Pro	Tyr	Ile	Arg	Ala	Glu	Va1	Glu	Asp	Asn	Ile	Met	Val	Thr
193	865					870					875					880
195	Phe	Arg	Asn	Gln	Ala	Ser	Arg	Pro	Tyr	Ser	Phe	Tyr	Ser	Ser	Leu	Ile
196		-			885		-			890					895	
198	Ser	Tvr	Glu	Glu	asp	Gln	Arg	Gln	Glv	Ala	Glu	Pro	Arg	Lys	Asn	Phe
199		4		900	•		_		905				_	910		
	Val	Lvs	Pro		G111	Thr	Lvs	Thr		Phe	Tro	Lvs	Va1		His	His
202	, 42	2,5	915	11011	O.L.		2,0	920	-1-	1 110	+	2,2	925	0111		
	Met	7 l a		Thr	Tara	Acn	C111		7 an	Cvc	Tue	7 l a		λΊэ	Ttrr	Dho
	Mec		PIO	TIII	цуѕ	кэр		FILE	АЗР	Cys	пуэ		тъ	AIG	тут	FILE
205	_	930		_	_		935	_			. .	940	-	- 3 -	a 1	.
	Ser	Asp	Val	Asp	Leu		Lys	Asp	Val	Hls		GTĀ	Leu	тте	GIY	
208						950		_			955	_	_			960
	Leu	Leu	Val	Cys		Thr	Asn	Thr	Leu		Pro	Ala	His	GLY		GIn
211					965					970					975	
213	Val	Thr	Val	Gln	Glu	Phe	Ala	Leu	Phe	Phe	Thr	Ile	Phe	Asp	Glu	Thr
214				980					985					990		
216	Lys	Ser	Trp	Tyr	Phe	Thr	Glu	Asn	Met	Glu	Arg	Asn	Cys	Arg	Ala	Pro
217	-		995	_				.000			-		.005	-		
	Cys	Asn	Ile	Gln	Met	Glu	Asp	Pro	Thr	Phe	Lys	Glu	Asn	Tyr	Arg	Phe
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Output Set: N:\CRF3\12172001\J006091.raw

220	1010					1015				-	1020				
	His Ala	Tlo	Nen	G1 v	η. 17.7.Υ		Met	Aen	Thr	T.A.II		Glv	T.e.ii	Va1	Met
	1025	116		Gry			nec	лор		1035		017	Leu		1040
	Ala Gln	Nan					Фrn	ጥህታ				Met	Glv		
225	Ala Gin	нэр		L045	116	Alg	пр		L050	пец	Ser	MCC		1055	11511
	Glu Asn	Tla			т1 о	uio	Dho			пiс	17 a 1	Dha			Δτα
	GIU ASII		H15	261	116	urs		1065	GTÄ	nrs	vaı		1111	vai	n19
229	Lys Lys			M	7	Mot			(I) 7 4 7 7	A an	T OU			C117	1721
					гуз		1080		ıyı			191 1085	PIO	СТУ	Val
232		1075											Ten	7 200	17-1
	Phe Glu	Tnr	Val	GIU			PLO	ser	цуѕ			TTE	тър	ALG	Val
235	1090	*	-3 -	01		1095	T	774 -	330		1100	C02	mh.»	Tou	Dho
	Glu Cys					HIS	ьeu	HIS			мес	Ser	1111		1120
	1105	_	~		TTT0	a	a1	m1		1115	a1	1404	* 1 -		
	Leu Val	Tyr			rys	Cys	GIN			Leu	СТУ	мес			СТХ
241		_		L125	~ 1	- 1	en1		L130	01	a1	m		1135	·
	His Ile	_	_	Phe	GIn	тте			ser	GTÄ	GIN			GIN	ттр
244			L140	_ •	_	_		1145	_	-1	_		L150	. 1 .	
	Ala Pro		Leu	Ala	Arg	Leu	His	Tyr	ser	GIY			Asn	Ата	Trp
247		1155				_ :			_			1165	_	- 1	n -
	Ser Thr	Lys	Glu	Pro			Trp	ITE	Lys			Leu	Leu	Ala	Pro
250	1170					1175			~3		1180		_	5 1	a
	Met Ile					Lys	Thr	GIn			Arg	GIn	ьуs		
	1185	_			1190	_,	_ 1			1195	_	_			L200
	Ser Leu	Tyr			GIn	Phe	He			Tyr	Ser	Leu			гĀг
256	_	_ •		L205	_		_		1210	43	1	_		L215	nl
	Lys Trp			Tyr	Arg	Gly			Thr	GIY	Thr			vaı	Pne
259			L220	_	_	_		1225	_		_		L230	•	D
	Phe Gly		Val	Asp	Ser								Pne	Asn	Pro
262		1235	- -	_	_		1240					L245	_	~	-1.
	Pro Ile	He	Ala	Arg								HIS	Tyr	ser	TTE
265		•	_	_		1255					1260	_		a	G
	Arg Ser	Thr	Leu	_		GLu	ьeu	мет			Asp	Leu	ASI	ser	Cys
	1265	_	_		1270	a 7				L275				1	
	Ser Met	Pro			Met	GLu	ser								тте
271		_		L285			_		L290		— 1			L295	a
	Thr Ala			Tyr	Phe	Thr			Phe	Ala				Pro	ser
274	_		L300					1305	_	_			1310	_	~ 1
	Lys Ala		Leu	His	Leu			Arg.	Ser	Asn			Arg	Pro	GIN
277		1315					1320			_	_	L325	_	1	
	Val Asn													Thr	met
	1330													_,	_
	Lys Val	Thr	Gly			Thr	GIn	GLY			Ser	Leu	Leu		
	1345	_			L350	_		_	_	1355		_	~ 1		1360
	Met Tyr	Val			Phe	Leu	Ile			Ser	GIn	Asp			GIn
286				L365		_			L370	_				1375	
	Trp Thr			Phe	Gln	Asn			Val	Lys	Val			GTĀ	Asn
289	=		L380		_			L385	_	_	_		1390	-	-
	Gln Asp		Phe	Thr	Pro			Asn	Ser	Leu			Pro	Leu	ьeu
292	-	1395]	L400				_	L405			

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317 ggggggcgct gcgcgggcgc agccatgcgt gaccgtgatg ag

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294 Thr Arg Tyr Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala 295 1410 1415 1420 297 Leu Arg Met Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr 298 1425 1430 1435 301 <210> SEQ ID NO: 2 302 <211> LENGTH: 402 303 <212> TYPE: DNA 304 <213> ORGANISM: Artificial Sequence 306 <220> FEATURE: 307 <223> OTHER INFORMATION: Description of Artificial Sequence: Derived from 308 Epstein-Barr virus sequence 310 <400> SEQUENCE: 2 311 ggcaatggag cgtgacgaag ggccccaggg ctgaccccgg caaacgtgac ccggggctcc 60 312 ggggtgaccc aggcaagcgt ggccaagggg cccgtgggtg acacaggcaa ccctgacaaa 120 313 ggccccccag gaaagacccc cggggggcat cgggggggtg ttggcgggtc atgggggggg 180 314 cgggtcatgc cgcgcattcc tggaaaaagt ggagggggg tggccttccc cccgcggccc 240 315 cetagecece eegeagagag eggegeaaeg gegggegage ggeggggggt eggggteege 300 316 gggctccggg ggctgcgggc ggtggatggc ggctggcgtt ccggggatcg gggggggtc 360

VERIFICATION SUMMARY

DATE: 12/17/2001

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Input Set : A:\MSB-7255.1.txt

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